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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	17

DATE MAILED: 10/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/870,353	WANG ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-8 and 11-42* is/are pending in the application.

4a) Of the above claim(s) *1,4-8 and 11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9,10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants cancellation of claims 2, 3, 9 and 10 and addition of new claims 15-42, Paper No. 15, 7/15/2003, is acknowledged. Claims 1, 4-8, 11-14 and 15-42 are at issue and are present for examination.

Applicant's election with traverse of Group II, Claims 15-428 in Paper No. 15 is acknowledged. The traversal is on the ground(s) that co-examination of all of Groups I-III would not require independent searches. This is not found persuasive because while the searches for the groups overlap, they are not coextensive. The search for Groups I and III would each require the search of subclasses unnecessary for the search of elected Group II. For example, search of Group I would require search of subclass 514/13 and search of Group III would require search of subclass 530/387.9

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 4-8, 11-14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 15.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-23 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that examination of Group II, drawn to a protein consisting of at least two heterologous domains wherein one of the domains is a non-specific nucleic acid binding domain and another is a catalytic acid modifying domain and group I, drawn to a method of amplifying a nucleic acid would not create an

undue burden. Applicants argument is not found persuasive because while the Groups are related and the searches for the each of the groups overlap, they are not coextensive. For example, search of Group II would require search of subclass 435/183 and 530/350, while the search of Group I would require search of subclass 435/6.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 4-8 and 11-14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 15.

Priority

Applicants statement on the first line of the specification to state that this application is a continuation in part of U.S. Application No. 09/640,958, filed August 16, 2000, which claims the priority of U.S. Provisional application 60/207,567, filed May 26, 2000, the disclosure of which is herein incorporated by reference is acknowledged.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosures, Paper No. 9, filed 1/14/2002, and Paper No. 10, filed 9/9/2002, is acknowledged. Those references considered have been initialed.

Claim Objections

Claim 40 is objected to because of the following informalities:

Claim 40 has two periods after the number "40.."

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 30 (claims 31-42 dependent on), 33 and 34 are indefinite in that the recitation "...identity to the Sac7d sequence set forth in SEQ ID NO: 10" is unclear. As applicants are using this recitation to structurally identify the genus of proteins encompassed by the claims, it is critical that that referred to region which applicants consider to be the Sac7d sequence set forth in SEQ ID NO: 10 is clear. While it is acknowledged that the Sac7d region of SEQ ID NO: 10 occurs at the amino terminal portion of SEQ ID NO: 10, the specific region specified remains unclear and thus those

domains which have 75, 85 or 95% identity to this region and are thus encompassed by the claims, remain unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-18 and 22-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 15-18 and 22-29 are directed to all possible proteins comprising two heterologous domains wherein the first domain is any sequence-non-specific-double-stranded nucleic–acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any DNA polymerase domain (claims 15-18 and 22-29).

The specification, however, only provides the representative species of Sso7d-delta*Taq*, Sso7d-*Taq*, and *Pfu*-Sso7d encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species with respect to those double-stranded nucleic acid binding domains which are capable of enhancing the processivity of an attached DNA polymerase domain beyond the full-length Sso7d protein. Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed

invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 15-29 and 30-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic–acid-binding domain is selected from the group consisting of Sso7d or Sac7d, does not reasonably provide enablement for any protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic–acid-binding domain comprises an amino acid sequence that has at least 50% identity to a 50 amino acid subsequence of SEQ ID NO: 2 or said sequence-non-specific-double-stranded nucleic–acid-binding domain comprises an amino acid sequence that has at least 75% identity to the Sac7d sequence set forth in SEQ ID NO: 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 5-29 and 30-42 are so broad as to encompass any protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic–acid-binding domain comprises an amino acid sequence that has at least 50%, 75% or 85% identity to a 50 amino acid subsequence of SEQ ID NO: 2 or specifically binds to polyclonal antibodies generated against Sso7d (claims 15-29) or said sequence-non-specific-double-stranded nucleic–acid-binding domain comprises an amino acid sequence that has at least 75% 85%, or 90% identity to the Sac7d sequence set forth in SEQ ID NO: 10 (claims 30-42). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins, specifically sequence-non-specific-double-stranded nucleic–acid-binding domains, broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, place in sufficient structural limits on the claimed sequence-non-specific-double-stranded nucleic–acid-binding domains. Since the amino acid

sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited those representative species of Sso7d-delta*Taq*, Sso7d-*Taq*, *Pfu*-Sso7d and Sac7d-delta*Taq* encompassed by these claims.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any protein comprising the encompassed modifications of the sequence-non-specific-double-stranded nucleic–acid-binding domains of Sso7d and Sac7d, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the sequence-non-specific-double-stranded nucleic–acid-binding activity; (B) the general tolerance of the

domains to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of said domains with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain function claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus having the claimed activities.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic–acid-binding domain comprises an amino acid sequence that has at least 50% identity to a 50 amino acid subsequence of SEQ ID NO: 2 or specifically binds to polyclonal antibodies generated against Sso7d, or said sequence-non-specific-double-stranded nucleic–acid-binding domain comprises an amino acid sequence that has at least 75% identity to the Sac7d

sequence set forth in SEQ ID NO: 10. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15-29 and 30-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 and 17-27, respectively, of U.S. Patent No. 6,627,424 B1. An obvious type double patenting rejection is appropriate where conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the claim is either anticipated by, or would have been obvious over, the reference claim(s). See,

e.g.., *In re* Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re* Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re* Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-16 and 17-27 of U.S. Patent No. 6,627,424 B1 drawn to a protein comprising at least two heterologous domains: a sequence non-specific double-stranded nucleic acid binding domain having at least 90% amino acid identity to SEQ ID NO: 2 (claims 1-16) or wherein the sequence non-specific double-stranded nucleic acid binding domain is Sac7d (claims 17-27) and a DNA polymerase domain, anticipates claims 15-29 and 30-42, respectively, of the instant application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.

Primary Examiner
Art Unit 1652

rgh
9/30/2003